

## Remarks

### **Amendments**

The claims have been amended to recite “biologically purified” instead of “isolated.” These are not narrowing amendments.

Amendments to the claims are made without prejudice or disclaimer. They are fully supported by the specification as filed and do not introduce new matter. Additionally, these amendments are not and should not be construed as admissions regarding the patentability of the claimed subject matter. Applicant reserves the right to pursue the subject matter of previously presented claims or any broader claims in this or in any other appropriate patent application. Accordingly, Applicant respectfully requests the entry of the amendments presented.

### **Request for Withdrawal of Final Rejection as Premature**

According to MPEP §706.07(a), a second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims, nor based on information submitted in certain information disclosure statements. The rejections of claims 9-15 and 21-23 are new grounds of rejection that were not necessitated by amendment of the claims or submission of an information disclosure statement. Therefore, the finality of the Office Action issued on June 22, 2010, is premature and Applicant respectfully requests withdrawal of the rejection.

### **Rejection of Claims 1-3, 5, 9-11, 13-15, 17-23, and 28-31 Under 35 U.S.C. § 112, first paragraph**

Claims 1-3, 5, 9-11, 13-15, 17-23, and 28-31 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. Applicant respectfully traverses the rejection.

Initially, Applicant has filed a request with the ATCC that the deposits of *S. oralis* strain ATCC SD-6229 and *S. uberis* strain ATCC SD-6228 be converted to deposits under the terms of the Budapest Treaty. The *S. oralis* strain ATCC SD-6229 and *S. uberis* strain ATCC SD-6228 strains will be irrevocably and without restriction or condition released to the public upon the issuance of a patent. Furthermore, as

previously mentioned, the ATCC sells many other strains of *S. oralis* and *S. uberis* including for example: ATCC 35037, ATCC 55229, ATCC 700233, ATCC 700234, ATCC 9811, ATCC 13386, ATCC 13387, ATCC 19435, ATCC 27958, ATCC 35648, ATCC 700407, ATCC 9927. Therefore, one of skill in the art could secure these strains during the life of the patent.

Regarding LDH-deficient *mutans streptococci* strains, the ATCC sells the following strains: *S. rattus* JH145 (ATCC 31377) and JH140 (ATCC 31341) (see specification page 8, first full paragraph). Furthermore, LDH-deficient *mutans streptococci* strains can be made using the methods disclosed in, for example, Hillman, "Lactate dehydrogenase mutants of *Streptococcus mutans*: isolation and preliminary characterization." Infect. Immun. 21:206-212 (1978) (of record). See also, specification page 8, first full paragraph. The Office asserts that there is "insufficient guidance described for obtaining these strains via the methods disclosed because of the unpredictability in the microbiological art." The Office additionally asserts that "there would be an undue burden of experimentation for one of ordinary skill in the art to have to carry out laborious methods for obtaining the strains and the expense involved." Applicant notes that the standard for written description does not include a consideration of: "undue burden of experimentation," "laborious methods," or "expense involved."

Rather, the standard for written description requires that a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991). The specification points to a thirty-two year old paper that describes how to make LDH-deficient *mutans streptococci* strains (Hillman, Lactate dehydrogenase mutants of *Streptococcus mutans*: isolation and preliminary characterization. Infect. Immun. 21:206-212 (1978) (of record)). Furthermore, those of skill in the art have indeed produced and reported on the construction of LDH-deficient *mutans streptococci* strains. See, e.g., Abhyankar *et al.*, "Serotype *c* *Streptococcus mutans* mutable to lactate dehydrogenase deficiency." J. Dent. Res. 64:1267 (1985) (copy attached); Kishimoto & Morioka, "High mutan and low

lactate-forming mutant of *Streptococcus mutans*.” J. Dent. Res. 60 (Special Issue B):1229 (1981) (copy attached); Salem *et al.*, “Lactate dehydrogenase-deficient mutants of serotype *g* *Streptococcus mutans*.” J. Dent. Res. 64:1191 (1985) (copy attached).

Additionally, *mutans streptococci* strains are very prevalent in the mouths of, e.g., humans and rats. See e.g., Okada *et al.* J. Med. Microbiol. 54:661 (2005) (copy attached); Twetman *et al.*, Oral Microbiol. Immun. 5:169 (1990) (abstract attached); Twetman *et al.*, Swed. Dent. J. 15:145 (1991) (abstract attached); Coykendall *et al.*, Infect. Immun. 10:216 (1974) (copy attached); Igarashi *et al.*, J. Med. Microbiol. 49:1069 (2000) (copy attached). As demonstrated by the prior art, one of skill in the art can isolate *mutans streptococci* strains from the mouths of humans or rats.

Therefore, because the specification provides details on the actual construction of LDH-deficient *mutans streptococci* strains, provides details on how to make additional LDH-deficient *mutans streptococci* strains, and those of skill in the art have been able to produce LDH-deficient *mutans streptococci* strains, the Applicant was clearly in possession of the invention. The microorganisms recited in the claims are readily available to the public and/or can be made using a repeatable process. As such, the specification provides adequate written description for the claims.

Applicant respectfully requests withdrawal of the rejection.

**Rejection of Claims 1-3, 5, 9-11, 13-15, 17-23, and 28-31 Under 35 U.S.C. § 112, first paragraph**

Claims 1-3, 5, 9-11, 13-15, 17-23, and 28-31 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. Applicant respectfully traverses the rejection.

The Office asserts that the specification is enabling for the specific strains of LDH-deficient *mutans streptococci* strains ATCC 31377 and ATCC 31341, but not for any and all strains that are LDH-deficient.

Under 35 U.S.C. § 112, all that is required for enablement is that the specification describe the invention in such terms as to enable a person skilled in the art to make and use the invention. The test of enablement is whether one reasonably skilled in the art (1) could make and use the invention (2) from the disclosures in the patent coupled with information known in the art (3) without undue experimentation. *In re Wands*, 858 F.2d

731 (Fed. Cir. 1988); *United States v. Telectronics, Inc.*, 857 F.2d 778 (Fed. Cir. 1988); M.P.E.P. § 2164.01.

Applicant submits that it is a matter of routine experimentation to make and screen *mutans streptococci* strains for lack of LDH activity using the techniques described in the specification and other well-known techniques. The law clearly states that "a considerable amount of experimentation is permissible, if it is merely routine." *In re Wands*, 858 F.3d 731, 737 (Fed. Cir. 1988). Furthermore, the fact that experimentation may be complex does not necessarily make it undue. *Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104 (Fed. Cir. 1985); *In re Wands*, 858 F.2d at 737 (Fed. Cir. 1988). Thus, the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498 (CCPA 1976).

The specification points to a thirty-two year old paper that describes how to make LDH-deficient *mutans streptococci* strains (Hillman, Lactate dehydrogenase mutants of *Streptococcus mutans*: isolation and preliminary characterization. *Infect. Immun.* 21:206-212 (1978)). Furthermore, those of skill in the art have indeed produced and reported on the construction of LDH-deficient *mutans streptococci* strains. See, e.g., Abhyankar *et al.*, "Serotype *c* *Streptococcus mutans* mutable to lactate dehydrogenase deficiency." *J. Dent. Res.* 64:1267 (1985) (copy attached); Kishimoto & Morioka, "High mutan and low lactate-forming mutant of *Streptococcus mutans*." *J. Dent. Res.* 60 (Special Issue B):1229 (1981) (copy attached); Salem *et al.*, "Lactate dehydrogenase-deficient mutants of serotype *g* *Streptococcus mutans*." *J. Dent. Res.* 64:1191 (1985) (copy attached). Specifically, Salem teaches that "[t]hree LDH-deficient mutants of a serotype *g* strain of *Streptococcus mutans* [now known as *S. sobrinus*] were produced essentially as described by Hillman (1978) [*Infect. Immun.* 21:206-212]." See abstract. Abhyankar *et al.* teaches the construction of "[t]hree lactate-dehydrogenase-deficient mutants of serotype *c* *S. mutans* [now known as *S. mutans*]." See abstract.

Additionally, *mutans streptococci* strains are very prevalent in the mouths of, e.g., humans and rats. See e.g., Okada *et al.* *J. Med. Microbiol.* 54:661 (2005) (copy attached); Twetman *et al.*, *Oral Microbiol. Immun.* 5:169 (1990) (abstract attached); Twetman *et al.*, *Swed. Dent. J.* 15:145 (1991) (abstract attached); Coykendall *et al.*,

Infect. Immun. 10:216 (1974) (copy attached); Igarashi *et al.*, J. Med. Microbiol. 49:1069 (2000) (copy attached). As demonstrated by the prior art, one of skill in the art can isolate *mutans streptococci* strains from the mouths of subjects.

Therefore, clearly, those of skill in the art could make and use LDH-deficient *mutans Streptococcus* strains without undue experimentation because several investigators have made such strains and published scientific articles reporting their results. Notably, these reports are at least twenty-five years old. Arguably, the art of genetic manipulation of microorganisms has advanced considerably in the last twenty-five years such that one of ordinary skill in the art could easily reproduce these results. The Office has provided no evidence or arguments as to why the construction of LDH-deficient *mutans streptococcus* strains would require undue experimentation. The claims are therefore enabled and Applicant respectfully requests withdrawal of the rejection.

**Rejection of Claims 1-3, 5, 9-11, 13-15, 17-23, and 28-31 Under 35 U.S.C. § 112, second paragraph**

Claims 1-3, 5, 9-11, 13-15, 17-23, and 28-31 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly lacking definiteness. Applicant respectfully traverses the rejection.

The Office asserts that the term “isolated” in the claims is not definite. Applicant respectfully disagrees. One of skill in the art would understand the meaning of an “isolated strain of bacteria.” In order to advance prosecution, however, Applicant has amended the claims to recite “biologically purified” instead of “isolated” according to the Office’s suggestion. This is not a narrowing amendment.

The claims are definite and Applicant respectfully requests withdrawal of the rejection.

**Rejection of Claims 1-3, 5, 9-11, 13-15, 17-23, and 28-31 Under 35 U.S.C. § 103(a)**

Claims 1-3, 5, 9-11, 13-15, 17-23, and 28-31 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over by EP0058575 in view of Tagg *et al.* Applicant respectfully traverses the rejection.

“[E]vidence of criticality or unexpected results, commercial success, long-felt but unsolved needs, failure of others, skepticism of experts, etc., must be considered by the

examiner in determining the issue of obviousness of claims for patentability under 35 U.S.C. 103." MPEP § 716.10(a). "[E]vidence rising out of the so-called 'secondary considerations' must always when present be considered en route to a determination of obviousness." *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983).

The claimed compositions and methods provide unexpected results in view of the cited art. The claimed combination of isolated bacterial strains provides an unexpected improvement or effect. It has been discovered that the claimed combination of bacterial strain unexpectedly promotes tooth whitening along with maintaining oral health (e.g., treatment, prevention or both treatment and prevention of periodontitis, dental caries, *Candida* or fungal overgrowth, halitosis, xerostomia-induced dental caries or periodontal disease, oral bacterial infections, oral bacterial disease, oral wounds or a combination thereof). See Declaration filed under 37 C.F.R. § 1.132 of Dr. Robert Zahradnik, ¶ 2, (filed herewith).

Stained dental ceramic material, representative of stained dental enamel, was treated with a suspension of *S. oralis* to determine if *S. oralis* can promote tooth whitening. See Declaration of Dr. Robert Zahradnik, ¶ 3. A suspension of *S. oralis* was incubated *in vitro* in the presence of glucose and oxygen, to determine if it could produce sufficient hydrogen peroxide to produce a measurable whitening effect on stained ceramic disks resembling teeth. The results are shown and discussed in paragraphs 4 to 8 of the Declaration of Dr. Robert Zahradnik. Briefly, *S. oralis* incubated in the presence of glucose and air produced a statistically significant whitening effect on tea and chlorhexidine-stained ceramic disks after 4 weeks of exposure to *S. oralis*. Inclusion of catalase in the incubation medium significantly reduced any whitening effect, suggesting that the mechanism of whitening involved hydrogen peroxide production by *S. oralis*. The whitening as a function of time did not plateau in this study (see Declaration, Figure 1, Group A), indicating that maximum whitening effect had not occurred within the timeframe of the study, and that longer treatment with *S. oralis* would likely achieve a greater whitening effect. See Declaration of Dr. Robert Zahradnik, ¶ 8.

The claimed combination of bacterial species provides an unexpected improvement or effect over the use of one species in isolation. Although the tooth

whitening data refers only to *S. oralis*, it is expected that the data provides a basis to predict that a combination of one or more *S. oralis*, *S. uberis*, and lactate dehydrogenase-deficient *mutans streptococcus* strains provides an advantage over using a single species in isolation. This is because different species of bacteria colonize different surfaces or portions of teeth. Therefore, the use of more than one species of bacteria can be used to “blanket” all or most surfaces of the teeth, whereas the use of only one species of bacteria may result in certain surfaces or portions of the teeth being uncolonized. Hillman *et al.* demonstrates that *S. oralis* (previously known as *S. sanguis*) and *S. mutans* have “physically distinct, non-overlapping niches” on teeth. J. Dent. Res. 66:1092 (1987); see page 1094; copy filed herewith. See Declaration of Dr. Robert Zahradnik, ¶ 9.

It was unexpected that bacteria, such as *S. oralis* and *S. uberis*, could produce hydrogen peroxide in an amount sufficient to actually whiten teeth along with providing oral health benefits such as the treatment, prevention, or both treatment and prevention of periodontitis, dental caries, *Candida* or fungal overgrowth, halitosis, xerostomia-induced dental caries or periodontal disease, oral bacterial infections, oral bacterial disease, oral wounds or a combination thereof. Therefore, it was unexpected, in light of the prior art, that a combination of *mutans streptococci* strains, wherein the *mutans streptococcus* strains are lactate dehydrogenase-deficient, *S. oralis* strains and *S. uberis* strains could be used to promote oral health and to promote cosmetic appearance by whitening teeth. See Declaration of Dr. Robert Zahradnik, ¶ 10.

The Office asserts that EP0058575 and Tagg together teach each of the claimed species and that each species is recognized by the cited art to use for the same intended purpose, treating oral cavities and oral diseases. As explained above, however, the instant invention provides results that would be viewed as surprisingly better or superior by a person of skill in the art. That is, it was not predictable or obvious that the claimed combination would provide oral health benefits along with the cosmetic benefits of teeth whitening.

Finally, neither EP0058575 nor Tagg teach the specific combinations of the invention. Tagg does not teach, suggest or even mention *S. uberis* and only teaches the use of *S. oralis* in a mixture of *S. sanguis* and *S. mitis*. See Table 1; page 220, left

col. Furthermore, each bacterium or group of bacteria mentioned by Tagg is taught to be useful for different types of treatments. See *e.g.*, Tagg, Table 1. EP0058575 and Tagg do not teach or suggest the specific combination of bacteria presently claimed in the instant invention.

Therefore, in view of the deficiencies of EP0058575 and Tagg and the unexpected and surprising results exhibited by the instantly claimed compositions and methods, the claims are not obvious over the cited art. Applicant respectfully requests withdrawal of the rejection.

Respectfully submitted,

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